

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 26571	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/IL 03/ 00711	International filing date (day/month/year) 28/08/2003	(Earliest) Priority Date (day/month/year) 30/08/2002
Applicant RAMOT AT TEL AVIV UNIVERSITY LTD.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 9 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

SELF-IMMOLATIVE DENDRIMERS RELEASING MANY ACTIVE MOIETIES UPON A SINGLE ACTIVATING EVENT

5. With regard to the **abstract**,

☐ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 2

☐ as suggested by the applicant.

☒ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT 03/00711

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61K47/48 C08G83/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 A61K C08G C08L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 19705 A (SQUIBB BRISTOL MYERS CO) 14 May 1998 (1998-05-14) page 13, line 17 - page 17, line 23; claims 22-44 and 49-57 ---	1-161
A	WO 98 13059 A (SQUIBB BRISTOL MYERS CO) 2 April 1998 (1998-04-02) page 12, lines 8-18; claims 1-3,12,22,23,27; figures 6-8 ---	1-161
A	ANTCZAK C ET AL: "A NEW ACIVICIN PRODRUG DESIGNED FOR TUMOR-TARGETED DELIVERY" BIOORGANIC & MEDICINAL CHEMISTRY, ELSEVIER SCIENCE LTD, GB, vol. 9, 2001, pages 2843-2848, XP001150714 ISSN: 0968-0896 abstract; scheme 1 --- -/--	1-161

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

16 December 2003

Date of mailing of the international search report

13/01/2004

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>NICULESCU-DUVAZ DAN ET AL: "Self-immolative nitrogen mustard prodrugs for suicide gene therapy" JOURNAL OF MEDICINAL CHEMISTRY, vol. 41, no. 26, 17 December 1998 (1998-12-17), pages 5297-5309, XP002265049 ISSN: 0022-2623 abstract; scheme 1; table 1 ---</p>	1-161
A	<p>TOKI BRIAN E ET AL: "Protease-mediated fragmentation of p-amidobenzyl ethers: A new strategy for the activation of anticancer prodrugs" JOURNAL OF ORGANIC CHEMISTRY, vol. 67, no. 6, 22 March 2002 (2002-03-22), pages 1866-1872, XP002265050 ISSN: 0022-3263 abstract; schemes 1-5; table 1; figure 1 ---</p>	1-161
A	<p>GROOT DE FRANCISCUS M H ET AL: "Elongated Multiple Electronic Cascade and Cyclization Spacer Systems in Activatable Anticancer Prodrugs for Enhanced Drug Release" JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY, EASTON, US, vol. 66, 2001, pages 8815-8830, XP002212035 ISSN: 0022-3263 abstract; page 8823, right-hand column, 4th paragraph; page 8824, left-hand column, 4th paragraph; schemes 1,5-7; figures 2,4 ---</p>	1-161
A	<p>GROOT DE F M H ET AL: "Synthesis and Biological Evaluation of 2'-Carbamate-Linked and 2'-Carbonate-Linked Prodrugs of Paclitaxel: Selective Activation by the Tumor-Associated Protease Plasmin" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 43, 2000, pages 3093-3102, XP002212034 ISSN: 0022-2623 abstract; chart 1; scheme 1 ---</p> <p style="text-align: center;">-/--</p>	1-161

INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A.	<p>WO 01 87348 A (UNIV MICHIGAN ;BAKER JAMES R JR (US); TOMALIA DONALD A (US)) 22 November 2001 (2001-11-22) paragraph joining pages 7 and 8; page 18, lines 11-23; page 25, line 30 - page 27, line 8; page 34, line 18 - page 35, line 33; figure 3; claims 1,3 -----</p>	1-161

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 103-118 and 147-160 are directed to methods of treatment and diagnosis practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition. The same observation apply to claims 119 and 121, which also relate to a diagnostic method practised in vivo.

Continuation of Box I.2

Claims Nos.: 1-161 (all partially)

Present claims 1-161 relate to an extremely large number of possible compounds, compositions containing them, as well as to their use and synthesis.

In particular, the compounds are defined by reference to a desirable characteristic or property, namely the self-immolation of the whole compound and its constitutive elements (i.e. the linker and eventually the spacer), which leads to the release of the tail units upon cleavage of the trigger unit (see for example claims 1, 3, 6 and 161).

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT) because a definition in terms of the results to be achieved is attempted.

In addition, the present set of claims fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) in view of the large number of the independent claims of the same categories (e.g.: claims 1 and 161, claims 119 and 122, claims 123, 130 and 137) and the large number of dependent claims, which merely redefine the same preferred features. The large number of claims renders difficult, if not impossible, to determine the matter for which protection is sought.

The present lack of clarity and support is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for the compounds with a 2,6-bis(hydroxymethyl)-p-cresol or 2,4,6-tris(hydroxymethyl)-phenol dendrimer structure. These compounds are mentioned in the examples and disclosed in figures 3-9, 13, 18, 20a, 22-26, 28, 31-33. With respect to claims 1-161, the search has been carried out in so far as the claims only relate to these compounds, i.e. the search has been carried out for the parts of the claims which appear to be clear, supported and disclosed.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL 03/00711

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 1-161 (all partially)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/03/00711

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9819705	A	14-05-1998	AU 5159798 A	29-05-1998
			CA 2264610 A1	14-05-1998
			EP 0941120 A1	15-09-1999
			JP 2001505194 T	17-04-2001
			WO 9819705 A1	14-05-1998
WO 9813059	A	02-04-1998	AU 739028 B2	04-10-2001
			AU 4599597 A	17-04-1998
			CA 2264227 A1	02-04-1998
			EP 0961619 A1	08-12-1999
			WO 9813059 A1	02-04-1998
WO 0187348	A	22-11-2001	US 6471968 B1	29-10-2002
			AU 6142001 A	26-11-2001
			CA 2408535 A1	22-11-2001
			EP 1301211 A2	16-04-2003
			WO 0187348 A2	22-11-2001
			US 2002165179 A1	07-11-2002